

Neonatal Necrotizing Enterocolitis

Clinical and Radiological Features

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NECROTIZING ENTEROCOLITIS is an often fatal inflammatory disease involving the intestinal tract of premature infants in which intestinal perforation is common. The condition may mimic obstruction both clinically and radiologically. Cases believed to represent this entity have been diagnosed diversely as neonatal appendicitis, peritonitis, colitis, ileitis, functional ileus, spontaneous ileal perforation, pneumatosis intestinale and portal vein gas.

This paper describes a retrospective study which was designed to analyze the clinical and radiological findings, therapy and prognosis in ten proven cases of neonatal necrotizing enterocolitis diagnosed over a three-year period. A further purpose of the study was to compare the contribution of the clinical history and physical findings with the role of radiology in making the diagnosis. An important question considered was whether the plain films of the abdomen would suffice in making the radiological diagnosis, or whether

barium contrast studies of the small bowel and colon provided sufficient additional information to warrant their use in all ill premature infants. A misleading finding in the barium contrast study of the small bowel, not previously reported, will be described.

Patients Studied

The radiographs and medical records were reviewed on all patients who had a surgical or pathological diagnosis of necrotizing enterocolitis during 1967-1970. Necrotizing enterocolitis was diagnosed in ten patients out of 2,492 admitted to the Sick Infant and Premature nurseries. Of the ten, five were born at Stanford Medical Center and five were transferred from other hospitals within the area.

Clinical Findings

Prenatal History

Only three of the mothers had no prenatal complications. Two mothers leaked amniotic fluid before delivery. Two others had vaginal bleeding during pregnancy and one of them received no prenatal care. One mother had placenta praevia. At delivery the amniotic fluid of one mother

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Necrotizing enterocolitis is an uncommon but dangerous disease in premature infants. Ten cases, seen over a three-year period at the Stanford University Medical Center, represented an incidence of 0.4 percent. The patients, six of whom died, derived from a general population, in contrast to the large series of patients reported in the literature in which the incidence was from 0.9 percent to 3.7 percent.³⁻⁶

The initial symptoms—rapid respiration, periodic breathing, lethargy and irritability—were identical to those which occurred in numerous infants who had respiratory disease. Subsequent symptoms (abdominal distension, in 100 percent; vomiting, 80 percent; apneic spells, 70 percent; jaundice, 70 percent; guaic-positive stools, 60 percent) were those of nonspecific acute abdominal disease.

The radiologist first made the diagnosis in 90 percent of cases. Interstitial air in the wall of the gut and the retroperitoneum, and portal vein gas were the most diagnostic radiographic features. Barium contrast studies were not helpful, and in one case led to the erroneous diagnosis of small bowel volvulus.

Plain abdominal radiographs must be taken of all premature infants with symptoms of nonspecific acute abdominal disease. If the radiographs are negative, but symptoms continue, they should be repeated at frequent intervals, for early diagnosis is critical to institution of proper therapy.

smelled foul; in another mother fever developed during an unsuccessful trial of labor that was terminated by cesarean section. Psychiatric problems requiring treatment with phenothiazines and other medications complicated one pregnancy.

Two babies were born by frank breech delivery and one by cesarean section. One was born in an automobile in the hospital parking lot.

Neonatal History

This series comprises six boys and four girls and includes four sets of twins. Only one twin in each pair contracted the disease. The mean birthweight of the affected infants was 1,576 grams with a standard deviation of 175 grams. Birthweight of the smallest infant was 1,050 grams while the heaviest infant weighed 2,409 grams. Only four patients weighed more than 1,600 grams. The mean gestational age was 32 weeks and the range was 28 to 38 weeks.

Neonatal problems other than prematurity occurred in all infants. All presented with respiratory problems including transient respiratory difficulty in two, periodic apneic pauses in one, aspiration pneumonia in two and respiratory distress syndrome in four. Cardiac catheterization demonstrated hypoplasia of the left heart with coarcta-

tion of the aorta distal to a patent ductus arteriosus in one patient who was symptomatic from birth with congestive heart failure.

Hyperbilirubinemia occurred in seven infants, two of whom required exchange transfusion. Some degree of acidosis, requiring correction, existed in most infants. In one baby omphalitis developed before onset of clinical symptoms. An umbilical vein catheter was introduced in two infants while seven received umbilical artery catheters.

Symptoms

Most infants had rapid respirations (greater than 60 to 70 breaths per minute), periodic breathing, lethargy and irritability before the onset of abdominal symptoms. These nonspecific symptoms also occurred in numerous infants who had respiratory disease and who did not subsequently have necrotizing enterocolitis. Symptoms suggesting abdominal disease appeared in six infants between the third and seventh day of life. Two infants were symptomatic on transfer to Stanford Medical Center from other hospitals on the eleventh and fifteenth days of life. Abdominal distension was observed in all infants as one of the earliest features. Vomiting and regurgitation occurred in eight infants; this phenomenon pre-

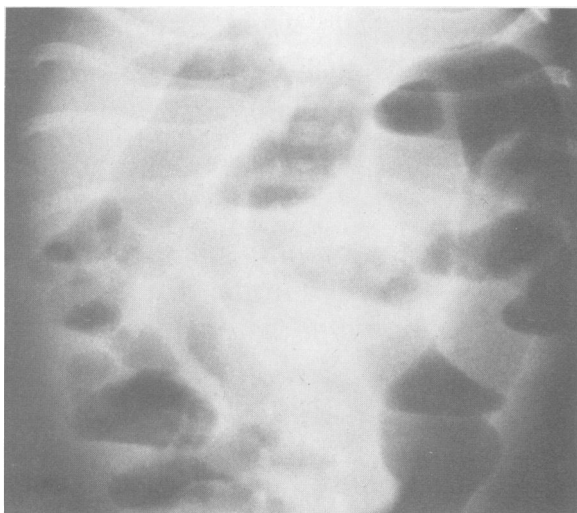


Figure 1.—Upright film of the abdomen showing gaseous distension of the bowel with multiple air fluid levels.

ceded abdominal distension by one day in two cases. Apneic episodes occurred in seven infants and seven appeared clinically jaundiced. Six babies passed guaic-positive stools.

Radiographic Features

Plain Film Features

Increased intraluminal gas and fluid were seen in all patients early in the course of the disease (Figure 1). Waxing and waning bouts of bowel distension occurred in two patients before the development of other more specific radiographic features at one month of age. In all ten patients there was a "bubbly" pattern which was sometimes localized to the right lower quadrant but frequently was more extensive and reflected the extent of the disease (Figure 2). Intramural gas occurred in nine patients (Figure 3). Hepatic portal venous gas was seen in eight (Figure 4); in one, it cleared over a period of several hours. Free intraperitoneal air was demonstrated in three patients (Figure 5).

Contrast Studies

Gastrointestinal contrast studies were performed on three patients. In one baby, the small bowel series was misleading and incorrectly suggested volvulus (Figure 6). Barium studies of the small bowel, performed through the gastrostomy tube in one of the patients, demonstrated segmental dilatation, narrowed segments, thickened folds and an irregular mucosal pattern. A barium enema study appeared normal in a third patient.



Figure 2.—Left flank with the patient supine showing a "bubbly" or "frothy" appearance to the bowel and curvilinear shadows indicating intramural gas.

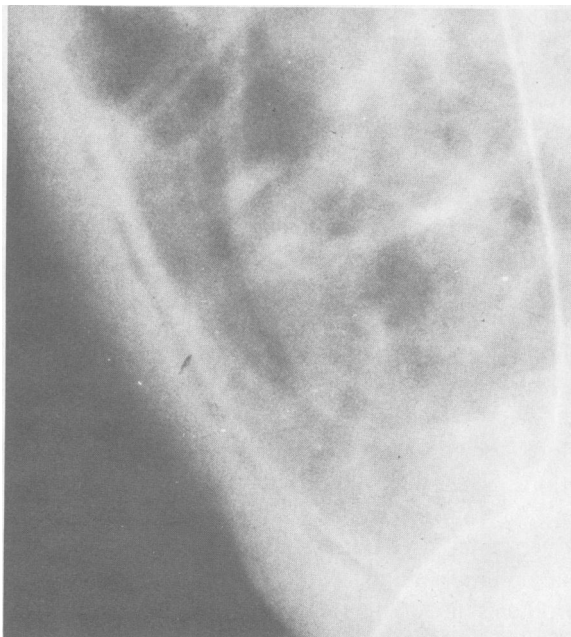


Figure 3.—Right flank with the patient supine showing streaks of intramural air in the cecum and ascending colon, and a thick linear streak of air in the properitoneal fat stripe.



Figure 4.—Liver, showing the typical appearance of gas in the portal venous system.

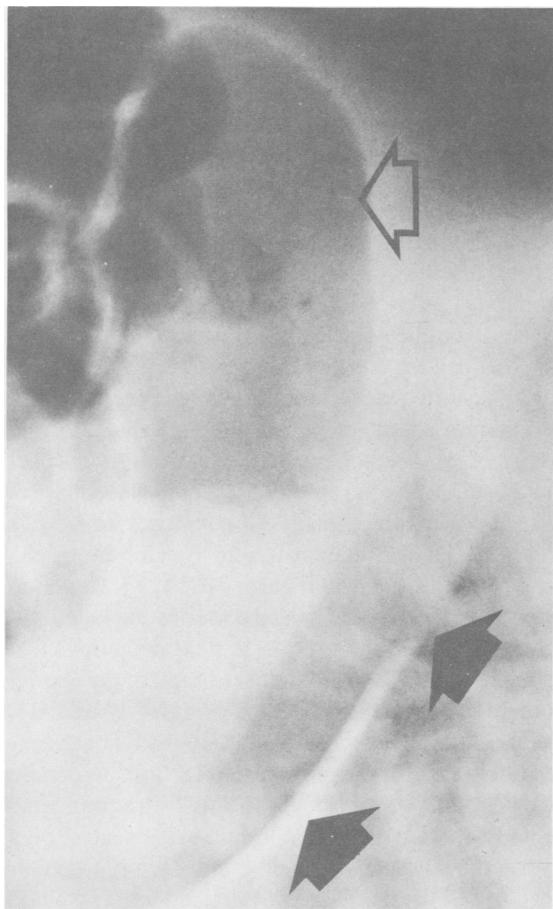


Figure 5.—Domes of the diaphragm with the patient supine and the film exposed using a horizontal beam. A large pneumoperitoneum is present (closed arrows). Fluid levels are present in the gut. A faint shadow of gas in the portal venous system can be seen (open arrow).

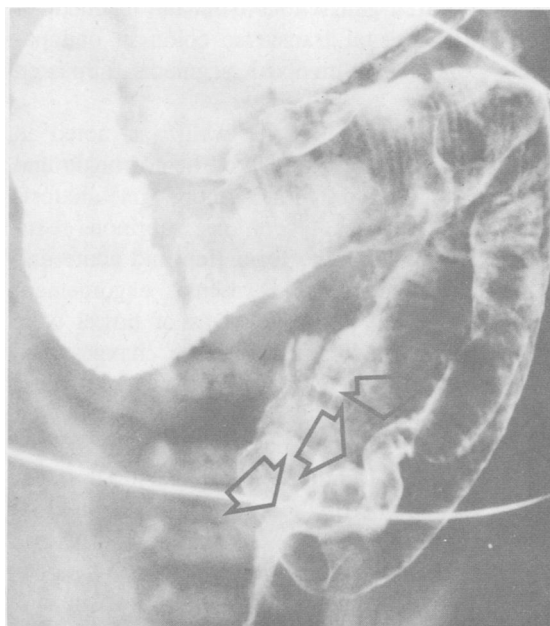


Figure 6.—Small bowel series. The upper jejunum is dilated. Barium did not pass beyond the upper quarter of the jejunum. At the site of obstruction the gut has a helical appearance (open arrows) suggesting a volvulus along the longitudinal axis. Gas is visible in gut distal to the obstruction. At operation extensive necrotizing enterocolitis was present but no volvulus was found.

Treatment

Nine patients were treated surgically. The other, who had congenital heart disease, was treated medically. Medical management consisted of bowel decompression, appropriate broad spectrum antibiotic therapy, respiratory assistance, maintenance of electrolytes, fluids and acid base balance, and maintenance of a constant body temperature. The surgical procedures varied and were primarily determined by the patient's condition and the pathologic situation encountered.

Pathology

Pathological findings varied, reflecting the extent and severity of the disease. Short segments of small bowel or cecum were affected in four patients but in the majority the disease involved one-half to one-third of the small bowel. The bowel appeared gangrenous from the ligament of Treitz to the distal transverse colon in one patient. Commonly, involved segments appeared dilated.

Decidedly thinned bowel wall was noted in some areas; the latter appeared hemorrhagic and bluish-gray in color. Furthermore, pneumatosis intestinale, mucosal ulcerations, fibrinous exudates, pseudomembrane formation and acute and chronic inflammation and vascular engorgement were present. The necrotic areas of bowel were clearly demarcated, and the tissue changes progressed in a manner similar to those of other ischemic diseases, suggesting that they were caused by mesenteric vasoconstriction. Portal vein gas and areas of perforation were found in some patients. Viewed microscopically, the bowel revealed hemorrhages into mucosa, lamina propria and serosa, infiltration of the interstitium by mononuclear cells, sloughing and ulceration of the surface epithelium, and areas of deep ulceration and perforation.

Bacterial Cultures

Blood or peritoneal cultures were positive in five patients. The gastric content, intestinal content or stool was positive in four. Organisms cultured were *E. coli* and the *Klebsiella aerobacter* group. In two patients, all cultures were sterile.

Prognosis

Six infants died, accounting for 5 percent of deaths from all causes in our nurseries during this period. A single patient, treated medically, died

but, because of the underlying heart disease, may not have survived regardless of the treatment employed. The three survivors were treated surgically.

Birthweight seemed to be a significant factor influencing survival: two of the three patients who survived weighed more than 1,500 grams at birth. Although positive blood cultures and hepatic portal venous gas usually portend death, blood and peritoneal cultures were positive in one survivor, while hepatic portal venous gas existed in two survivors. On the other hand no infants survived who had pneumoperitoneum.

All survivors are still living, and have been followed for periods of from two to 29 months. None are entirely normal. Two patients, who are gaining weight, have suffered from respiratory tract infections while one patient has iron deficiency anemia. One baby was readmitted to the hospital because of failure to thrive, the cause of which has not been discovered.

Discussion

In nine of the ten cases in this series, the radiologist first made the correct diagnosis. In two cases, the diagnosis was made from a chest radiograph. Clinical signs were those of nonspecific acute abdominal disease and usually appeared between the third and seventh day of life; the most common were vomiting, abdominal distension, apnea, jaundice and gastro-intestinal bleeding.

Recognition of the earliest radiological features is critical to the institution of proper therapy. Premature infants who have bowel dilatation or signs of obstruction must be particularly suspect (Figure 1) and further films should be obtained.

We have found plain film features to be the most useful for diagnosis and for following the course of the disease (Figures 2, 3, 4, 5). Common radiographic features in our series included increased intraluminal gas and fluid (Figure 1), a "bubbly" or "frothy" appearance to the bowel (Figure 2), intramural gas (Figures 2 and 3), hepatic portal venous gas (Figure 4) and pneumoperitoneum (Figure 5). We are uncertain whether the "bubbly" or "frothy" appearance so characteristic of this condition delineates only intramural gas or whether it represents a combination of intramural gas with mixed gas and blood in the bowel lumen. Contrast studies, performed in three infants, were of no value. In one case, the findings on a small bowel series were positively misleading (Figure 6). The value of barium enemas to exclude mechanical obstruction or angang-

lionirosis must be weighed against the potential hazard of perforation and extravasation of contrast medium into the peritoneum. Critically ill premature infants may be unable to tolerate contrast examinations.

In our experience, gas in the wall of the intestine, mesentery and retroperitoneum, and portal vein gas, are the most important and useful radiographic features. Neither is pathognomonic; both features have been observed in patients afflicted with such entities as Hirshsprung's disease, imperforate anus, meconium ileus, small bowel atresia and following surgical repair of coarctation of the aorta. Portal vein gas can be introduced inadvertently through umbilical vein catheters.¹ Pneumoperitoneum (Figure 5) and gas in the portal venous system (Figure 4)—both generally late findings—denote a poor prognosis. When originally described, portal vein gas was felt to be universally fatal² but subsequently survivors have been reported in whom portal vein gas was present. Two patients with this phenomenon in the present study survived.

The disease incidence at Stanford Medical Center during 1967-1970 was 0.4 percent. This is much lower than the incidence of *unequivocal* necrotizing enterocolitis reported from the two largest series, which ranged from 0.9 percent to 3.7 percent of all admissions to Premature and Sick Infant nurseries.³⁻⁶ The wide variation in incidence figures probably reflects population selection more than any other single factor. In the two largest series reported, the patients were admitted to special units, whereas the patients described in this paper were part of the general premature infant population.

The cause of the disease remains unknown, but several theories have been proposed: (1) Traumatic rupture of the bowel during delivery; (2) congenital defects of the bowel wall;⁷ (3) infection;⁸⁻¹⁰ (4) a localized Schwartzman reaction;¹¹ (5) vasoconstriction of the terminal mesenteric arterioles due to the combined action of bacterial endotoxins and elevated blood levels of catecholamines secondary to stress; (6) perinatal anoxia or hypoxia.¹²⁻¹⁵

There is probably no one cause. Despite the

multiple etiologic factors, the pathogenesis may be similar in all cases. Mesenteric vasoconstriction is important because the necrotic areas are clearly demarcated and the tissue changes progress in a fashion similar to that of other ischemic diseases.³⁻⁵ The surgical and autopsy findings in our series support the contention that spasm of the mesenteric vessels leads to necrosis of the bowel.

Conclusion

Early diagnosis is critical to the institution of proper therapy in premature infants with necrotizing enterocolitis. In order to make the early diagnosis of necrotizing enterocolitis, plain abdominal radiographs must be taken of all premature infants with abdominal distension, vomiting, apneic spells, jaundice, or guaiac-positive stools. If the radiographs are negative, but symptoms continue, they should be repeated. Barium contrast studies of the small bowel and colon are of no value in making the diagnosis, and can be misleading.

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